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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/630,968	07/31/2003	John J. Rossi	1954-401	3645

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ROTHWELL, FIGG, ERNST & MANBECK, P.C.
1425 K STREET, N.W.
SUITE 800
WASHINGTON, DC 20005

EXAMINER	
SHIN, DANA H	

ART UNIT	PAPER NUMBER
1635	

NOTIFICATION DATE	DELIVERY MODE
07/08/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

Office Action Summary	Application No.	Applicant(s)	
	10/630,968	ROSSI ET AL.	
	Examiner	Art Unit	
	DANA SHIN	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,17,19-23 and 30-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,17,19-23 and 30-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 July 2003 and 24 November 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 13, 2009 has been entered.

Status of Claims

Claims 1-9, 17, 19-23, and 30-32 are pending and under examination on the merits in the instant case.

Response to Arguments

Applicant's arguments with respect to claims 1-9, 17, 19-23, and 30-32 filed with the RCE have been considered but are moot in view of the new ground(s) of rejection. See below.

Priority

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed applications, Application Nos. 60/399,718 and 60/408,298, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. The disclosure of 60/399,718 and 60/408,298 provides adequate support for a U6 promoter-containing siRNA expression cassette but not U1 or H1 promoter-containing siRNA expression cassette or a mammalian Pol II promoter that is specifically claimed in claims 30-32. Hence, the benefit of an earlier filing date is denied for claims 30-32 and therefore the instant filing date of July 31, 2003 will be the effective filing date for claims 30-32.

If applicant believes that the claimed subject matter in claims 30-32 is adequately supported by the disclosure of either priority applications, applicant is advised to point out the particulars in response to this Office action.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-9, 17, 19-23, and 30-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shi et al. (US 2003/0180756 A1) in view of Medina et al. (*Nucleic Acids Research,* 1999, 27:1698-1708) and Dietz (US 5,814,500, citation of record).

The claims are drawn to a PCR amplification-based method for producing a mammalian promoter-containing siRNA expression cassette comprising treating one strand sequence of a double-stranded mammalian promoter sequence with an oligonucleotide primer complementary to the 5' end of the promoter sequence that transcribes an siRNA molecule in mammalian cells, treating the other strand of the promoter sequence with an oligonucleotide primer complementary to the 3' end of the promoter sequence, an antisense sequence of an siRNA molecule, and a termination sequence of 4-6 deoxyadenosines, further comprising a tag sequence for identifying functional siRNA, wherein the tag sequence comprises a restriction site for cloning, wherein the promoter is a human U6 or H1 or U1 snRNA promoter, wherein the method further comprises a transfection step wherein the siRNA molecule is expressed in mammalian cells *in vitro* and further comprises a screening step for a target site on mRNA for siRNA targeting, wherein the

transfection is performed with two or more different siRNA expression cassettes, wherein the primers are modified by phosphorylation.

Shi et al. teach a method for producing siRNA molecules in a mammalian cell *in vitro* by preparing an expression vector comprising a mammalian RNA polymerase III promoter such as a U6 or H1 RNA promoter or a polymerase II promoter, wherein a double-stranded nucleic acid sequence encoding an siRNA molecule and a transcriptional termination signal sequence of five deoxythymidines are inserted into the expression vector at a restriction enzyme recognition site by cloning/ligation methodologies. They teach that transfection of the mammalian RNA polymerase III promoter-containing expression vector results in efficient siRNA-mediated target gene silencing in cultured mammalian cell lines *in vitro*. See paragraphs 0014-0017, 0058, 0068, 0078, 0087-0095, 0189-0219; claims 49-54. Note that all of the teachings of Shi et al. described herein are adequately supported by the earliest filed priority application, Application No. 60/366,478, filed on March 21, 2002.

Medina et al. teach a method of generating a library expression vector comprising a T7 promoter operably linked to a ribozyme by using a PCR-based amplification method comprising a 5' primer to amplify the promoter sequence and the 5' half of the ribozyme sequence and a 3' primer to amplify the 3' half of the ribozyme sequence, wherein some regions of the ribozyme are double-stranded, and wherein the primers also include restriction enzyme cleavage site sequences, wherein the PCR-amplified ribozyme library expression vector is transcribed in cells. They teach that the PCR-amplified ribozyme production and expression method allows one of ordinary skill in the art to identify effective ribozyme sequences. See the entire reference including Figures 2A and 2B.

Dietz teaches a U1 snRNA promoter-containing expression vector wherein the U1 snRNA promoter drives and transcribes the expression of a ribozyme in a cell transfected with the expression vector. See the entire reference.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a mammalian promoter-linked siRNA expression vector of Shi et al. by replacing the ligation/cloning methodology of Shi et al. with the PCR-based amplification methodology of Medina et al.

One of ordinary skill in the art would have been motivated to produce siRNA expression vectors by amplifying the nucleotide sequences of the vector elements including the promoter-encoding nucleotide sequence, siRNA-encoding nucleotide sequence, and a transcriptional termination signal sequence with appropriate nucleotide sequence-specific primers that are able to amplify the nucleotide sequences in a PCR-based amplification mechanism, because producing short RNA inhibitor molecules by making a promoter-containing expression vector through a PCR-based amplification method was known to allow one to rapidly identify effective RNA inhibitor sequences as taught by Medina et al. Since the two known methodologies, a ligation/cloning methodology and a PCR-amplification methodology, for making a promoter-containing expression vector comprising an RNA molecule were known to be functionally equivalent and therefore interchangeable, and since the potential benefits of the PCR-based amplification methodology in saving time, expenses, and labor compared to cloning/ligation methodology would have been apparent to one of ordinary skill in the art, and since the principles and skills required to make appropriate primers and use a PCR-based amplification method were well-known and thus within the technical grasp of one of ordinary skill in the art at

the time the invention was made, one of ordinary skill in the art would have had a reasonable expectation of success in producing a mammalian pol III-containing siRNA expression cassette by a PCR-based amplification method. In addition, since a U1 snRNA promoter was known to be capable of transcribing a short RNA inhibitor molecule as the U6 or H1 promoter, thereby suggesting that the U1 snRNA promoter of Dietz is functionally equivalent and interchangeable with the U6 or H1 promoter of Shi et al. for transcribing and expressing an siRNA molecule in cells, one of ordinary skill in the art would have been motivated to use any one of the art-recognized promoters with a reasonable expectation of success. Accordingly, the claimed invention taken as a whole would have been *prima facie* obvious at the time of filing.

Claims 30-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Engelke et al. (US 2003/0148519 A1, citation of record) in view of Caplan et al. (US 2003/0149113 A1) and Kreutzer et al. (US 2004/0001811 A1).

The claims are drawn to an amplification-based method for producing a mammalian promoter-containing siRNA expression cassette, wherein the mammalian promoter is a U6 or H1 or U1 snRNA promoter.

Engelke et al. teach that one can synthesize an expression vector comprising a mammalian promoter-driven siRNA by a PCR amplification method instead of a more conventional cloning method. They teach that the PCR synthesis method allows rapid screening for identifying effective siRNA insert sequences. They teach that the mammalian promoter includes a U6 promoter. See paragraphs 0177, 0194-0196. Engelke et al. do not teach a mammalian H1 promoter or U1 snRNA promoter.

Caplan et al. teach an siRNA expression vector comprising a U6 or H1 promoter. See paragraph 0183.

Kreutzer et al. teach that an siRNA expression vector can comprise a U1 snRNA promoter to drive the expression of the siRNA molecule. See paragraphs 0006, 0089.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to replace the U6 promoter of Engelke et al. with the H1 promoter or U1 snRNA promoter in the PCR-amplification method for producing a mammalian promoter-containing siRNA expression vector of Engelke et al.

One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success because the H1 promoter and the U1 snRNA promoter and the U6 promoter were each known to transcribe and express siRNA molecules when the promoter-containing siRNA expression vector is transfected into cells, thereby suggesting that the three art-recognized promoters are functionally equivalent and thus interchangeable without affecting the siRNA expression in cells. Note that substituting art-recognized equivalents known for the same purpose is a well-established rationale in support of an obviousness rejection. See MPEP 2144.06. Accordingly, the claimed invention taken as a whole would have been *prima facie* obvious at the time of filing.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DANA SHIN whose telephone number is (571)272-8008. The examiner can normally be reached on Monday through Friday, 7am-3:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Dana Shin
Examiner
Art Unit 1635

/Dana Shin/
Examiner, Art Unit 1635